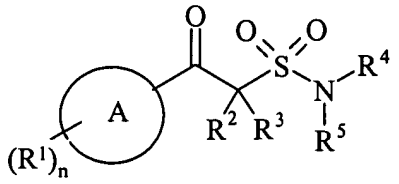
AMENDMENTS TO THE CLAIMS

Claims

1. (Currently Amended) ~~The use of~~A method for inhibiting 11βHSD1, comprising administering a compound of formula **(I)**:



(I)

wherein[[:]]

Ring A is selected from carbocyclyl or heterocyclyl;

each $\mathbf{R^1}$ is independently selected from halo, nitro, cyano, hydroxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{1-4}alkoxy, C_{1-4}alkanoyl, C_{1-4}alkanoyloxy, *N*-(C_{1-4}alkyl)amino, *N,N*-(C_{1-4}alkyl)$_2$amino, C_{1-4}alkanoylamino, *N*-(C_{1-4}alkyl)carbamoyl, *N,N*-(C_{1-4}alkyl)$_2$carbamoyl, C_{1-4}alkylS(O)$_a$ wherein a is 0 to 2, C_{1-4}alkoxycarbonyl, *N*-(C_{1-4}alkyl)sulphamoyl, *N,N*-(C_{1-4}alkyl)$_2$sulphamoyl, C_{1-4}alkylsulphonylamino, tri-(C_{1-4}alkyl)silyloxy, carbocyclyl, heterocyclyl, carbocyclylC_{0-4}alkylene-Y-, and heterocyclylC_{0-4}alkylene-Y-; wherein R^1 may be optionally substituted on carbon ~~by~~ with one or more R^6 groups ~~selected from R^6~~; and wherein if said heterocyclyl contains an -NH- moiety, that nitrogen may be optionally substituted ~~by~~ with an R^7 group ~~selected from R^7~~;

n is 0-5; ~~wherein the values of R^1 may be the same or different;~~

$\mathbf{R^2}$ and $\mathbf{R^3}$ are independently selected from hydrogen, hydroxy, amino, cyano, C_{1-4}alkyl, C_{1-4}alkoxy, *N*-(C_{1-4}alkyl)amino, *N,N*-(C_{1-4}alkyl)$_2$amino, carbocyclyl, heterocyclyl, carbocyclylC_{1-4}alkyl, and heterocyclylC_{1-4}alkyl; or R^2 and R^3 together ~~form~~ are C_{2-6}alkylene; wherein R^2 and R^3 may be independently optionally substituted on carbon ~~by~~ with one or more R^8 groups ~~selected from R^8~~; and wherein if said heterocyclyl contains an -NH- moiety, that nitrogen may be optionally substituted ~~by~~ with an R^9 group ~~selected from R^9~~;

one of **R**[4] and **R**[5] is ~~selected from~~ C_{1-4}alkyl and the other is selected from hydrogen ~~or~~ and C_{1-4}alkyl; wherein R^4 and R^5 may be optionally substituted on carbon ~~by~~ with one or more R^{10} groups ~~selected from R^{10}~~;

Y is selected from $-S(O)_a-$, -O-, $-NR^{12}-$, -C(O), $-C(O)NR^{13}-$, $-NR^{14}C(O)-$, and ~~or~~ $-SO_2NR^{15}-$; wherein a is 0 to 2;

R[12], **R**[13], **R**[14] and **R**[15] are independently selected from hydrogen, phenyl, and C_{1-4}alkyl;

R[6] and **R**[8] are independently selected from halo, nitro, cyano, hydroxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, trifluoromethyl, trifluoromethoxy, C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{1-4}alkoxy, C_{1-4}alkanoyl, C_{1-4}alkanoyloxy, *N*-(C_{1-4}alkyl)amino, *N,N*-(C_{1-4}alkyl)$_2$amino, C_{1-4}alkanoylamino, *N*-(C_{1-4}alkyl)carbamoyl, *N,N*-(C_{1-4}alkyl)$_2$carbamoyl, C_{1-4}alkyl$S(O)_a$ wherein a is 0 to 2, C_{1-4}alkoxycarbonyl, *N*-(C_{1-4}alkyl)sulphamoyl, *N,N*-(C_{1-4}alkyl)$_2$sulphamoyl, C_{1-4}alkylsulphonylamino, carbocyclyl, and heterocyclyl; wherein R^6 and R^8 may be independently optionally substituted on carbon ~~by~~ with one or more R^{11} groups;

R[10] is selected from halo, nitro, cyano, hydroxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, trifluoromethyl, trifluoromethoxy, C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{1-4}alkoxy, C_{1-4}alkanoyl, C_{1-4}alkanoyloxy, *N*-(C_{1-4}alkyl)amino, *N,N*-(C_{1-4}alkyl)$_2$amino, C_{1-4}alkanoylamino, *N*-(C_{1-4}alkyl)carbamoyl, *N,N*-(C_{1-4}alkyl)$_2$carbamoyl, C_{1-4}alkyl$S(O)_a$ wherein a is 0 to 2, C_{1-4}alkoxycarbonyl, *N*-(C_{1-4}alkyl)sulphamoyl, *N,N*-(C_{1-4}alkyl)$_2$sulphamoyl, and C_{1-4}alkylsulphonylamino; wherein R^{10} may be independently optionally substituted on carbon ~~by~~ with one or more R^{16} groups;

R[7] and **R**[9] are independently selected from C_{1-4}alkyl, C_{1-4}alkanoyl, C_{1-4}alkylsulphonyl, C_{1-4}alkoxycarbonyl, carbamoyl, *N*-(C_{1-4}alkyl)carbamoyl, *N,N*-(C_{1-4}alkyl)$_2$carbamoyl, benzyl, benzyloxycarbonyl, benzoyl, and phenylsulphonyl;

R[11] and **R**[16] are independently selected from halo, nitro, cyano, hydroxy, trifluoromethoxy, trifluoromethyl, amino, carboxy, carbamoyl, mercapto, sulphamoyl, methyl, ethyl, methoxy, ethoxy, acetyl, acetoxy, methylamino, ethylamino, dimethylamino, diethylamino, *N*-methyl-*N*-ethylamino, acetylamino, *N*-methylcarbamoyl, *N*-ethylcarbamoyl, *N,N*-dimethylcarbamoyl, *N,N*-diethylcarbamoyl, *N*-methyl-*N*-ethylcarbamoyl, methylthio, ethylthio, methylsulphinyl, ethylsulphinyl, mesyl, ethylsulphonyl, methoxycarbonyl, ethoxycarbonyl, *N*-methylsulphamoyl, *N*-ethylsulphamoyl, *N,N*-dimethylsulphamoyl, *N,N*-diethylsulphamoyl, and ~~or~~ *N*-methyl-*N*-ethylsulphamoyl;

or a pharmaceutically acceptable salt thereof~~;~~

~~in the manufacture of a medicament for use in the inhibition of 11βHSD1~~.

2. (Currently Amended) ~~The use~~ A method according to claim 1 wherein Ring A is selected from pyridyl, phenyl, thienyl, furyl, pyrazinyl, 1,2,3-thiadiazolyl, thiazolyl, cyclohexyl, naphthyl, cyclohexenyl, pyrazolyl, benzothienyl, indolyl, 1,1,3-trioxo-2,3-dihydro-1,2-benzisothiazolyl, 1,3-benzodioxolyl, cyclopentyl, tetrahydropyranyl, 1-oxooctahydropyrido[1,2-a]pyrazinyl, 1,2,3,4-tetrahydronaphthyl, piperidinyl, and benzthiazolyl.

3. (Currently Amended) ~~The use~~ A method according to ~~either of~~ claims 1 ~~or 2~~ wherein each R^1 is independently selected from halo, nitro, cyano, sulphamoyl, C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{1-4}alkoxy, C_{1-4}alkanoyl, tri-(C_{1-4}alkyl)silyloxy, carbocyclyl, and heterocyclylC_{0-4}alkylene-Y-; wherein R^1 may be optionally substituted on carbon ~~by~~ with one or more R^6 groups ~~selected from R^6~~; ~~wherein~~

Y is -NR^{12}-;

R^{12} is hydrogen; and

R^6 is selected from halo, C_{2-4}alkenyl, C_{1-4}alkanoyl, C_{1-4}alkanoylamino, and carbocyclyl.

4. (Currently Amended) ~~The use~~A method according to ~~any one of~~ claims 1 ~~-4~~ wherein n is 0-2~~; wherein the values of R^1 may be the same or different~~.

5. (Currently Amended) ~~The use~~A method according to ~~any one of~~ claims 1 ~~-5~~ wherein R^2 and R^3 are independently selected from hydrogen ~~or~~ and C_{1-4}alkyl[[,]]; or R^2 and R^3 together ~~form~~ are C_{2-6}alkylene.

6. (Currently Amended) ~~The use~~A method according to ~~any one of~~ claims 1 ~~-6~~ wherein ~~one of R^4 and R^5 is selected from hydrogen and C_{1-4}alkyl and the other is selected from C_{1-4}alkyl; wherein R^4 and R^5 may be optionally substituted on carbon by one or more groups selected from R^{10}; and~~

———R^{10} is selected from C_{1-4}alkoxy and *N,N*-(C_{1-4}alkyl)$_2$amino.

7. (Currently Amended) ~~The of a~~ A method of~~compound of formula (I) (as depicted in~~ claim 1,~~)~~

wherein[[:]]

Ring A is selected from carbocyclyl ~~or~~ and heterocyclyl;

each R^1 is independently selected from halo, nitro, cyano, sulphamoyl, C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{1-4}alkoxy, C_{1-4}alkanoyl, tri-(C_{1-4}alkyl)silyloxy, carbocyclyl, and heterocyclylC_{0-4}alkylene-Y-; wherein R^1 may be optionally substituted on carbon ~~by~~ with one or more R^6 groups ~~selected from R^6~~; ~~wherein:~~

Y is -NR^{12}-;

R^{12} is hydrogen; ~~and~~

R^6 is selected from halo, C_{2-4}alkenyl, C_{1-4}alkanoyl, C_{1-4}alkanoylamino, and carbocyclyl;

n is 0-3; ~~wherein the values of R^1 may be the same or different;~~

R^2 and R^3 are independently selected from hydrogen ~~or~~ and C_{1-4}alkyl, or R^2 and R^3 together ~~form~~ are C_{2-6}alkylene;

one of R^4 and R^5 is selected from hydrogen and C_{1-4}alkyl and the other is ~~selected from~~ C_{1-4}alkyl; wherein R^4 and R^5 may be optionally substituted on carbon ~~by~~ with one or more R^{10} groups ~~selected from R^{10}~~; and

R^{10} is selected from C_{1-4}alkoxy and *N,N*-(C_{1-4}alkyl)$_2$amino;

or a pharmaceutically acceptable salt thereof;

~~in the manufacture of a medicament for use in the inhibition of 11βHSD1~~.

8. (Currently Amended) A compound ~~of formula (I) as depicted in claim 1~~ selected from:

(4-fluorophenyl)[*N*-(2-methoxyethyl)-*N*-(methyl)sulphamoylmethyl]ketone;

(2,4-difluorophenyl)[1-(*N,N*-diisopropylsulphamoyl)-1methylethyl]ketone;

(2,4-difluorophenyl)(*N,N*-diisopropylsulphamoylmethyl)ketone;

(thiazol-2-yl)(*N,N*-dimethysulphamoylmethyl)ketone;

(4-fluorophenyl)[*N*-(2-isopropoxyethyl)-*N*-(isopropyl)sulphamoylmethyl]ketone;

(pyrazin-2-yl)(*N,N*-dimethysulphamoylmethyl)ketone;

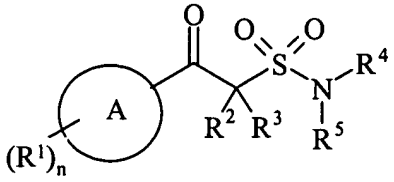
(4-isopropoxyphenyl)(*N,N*-diisopropylsulphamoylmethyl)ketone;

(3-cyanophenyl)(*N,N*-diisopropylsulphamoylmethyl)ketone; and

(pyrid-2-yl)(*N,N*-dimethysulphamoylmethyl)ketone;

or a pharmaceutically acceptable salt thereof.

9. (Currently Amended) A compound of formula **(Ia)**:



(Ia)

wherein[[:]]

Ring A is selected from phenyl, pyridyl, thiazolyl, thienyl, and furyl;

each $\mathbf{R^1}$ is independently selected from halo, nitro, cyano, hydroxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{1-4}alkoxy, C_{1-4}alkanoyl, C_{1-4}alkanoyloxy, *N*-(C_{1-4}alkyl)amino, *N,N*-(C_{1-4}alkyl)$_2$amino, C_{1-4}alkanoylamino, *N*-(C_{1-4}alkyl)carbamoyl, *N,N*-(C_{1-4}alkyl)$_2$carbamoyl, C_{1-4}alkylS(O)$_a$ wherein a is 0 to 2, C_{1-4}alkoxycarbonyl, *N*-(C_{1-4}alkyl)sulphamoyl, *N,N*-(C_{1-4}alkyl)$_2$sulphamoyl, and C_{1-4}alkylsulphonylamino; wherein R^1 may be optionally substituted on carbon ~~by~~ with one or more R^6 groups ~~selected from R^6~~; and wherein if said heterocyclyl contains an -NH- moiety, that nitrogen may be optionally substituted ~~by~~ with an R^7 group ~~selected from R^7~~;

n is 0-3; ~~wherein the values of R^1 may be the same or different;~~

$\mathbf{R^2}$ and $\mathbf{R^3}$ are independently selected from hydrogen, hydroxy, amino, cyano, C_{1-4}alkyl, C_{1-4}alkoxy, *N*-(C_{1-4}alkyl)amino, *N,N*-(C_{1-4}alkyl)$_2$amino, carbocyclyl, heterocyclyl, carbocyclylC_{1-4}alkyl, and heterocyclylC_{1-4}alkyl; wherein R^2 and R^3 may be independently optionally substituted on carbon ~~by~~ with one or more R^8 groups ~~selected from R^8~~; and wherein if said heterocyclyl contains an -NH- moiety, that nitrogen may be optionally substituted ~~by~~ with an R^9 group selected from ~~R^9~~;

$\mathbf{R^4}$ and $\mathbf{R^5}$ are independently ~~selected from~~ C_{1-4}alkyl; wherein R^4 and R^5 may be optionally substituted on carbon ~~by~~ with one or more R^{10} groups ~~selected from R^{10}~~;

$\mathbf{R^6}$ and $\mathbf{R^8}$ are independently selected from halo, nitro, cyano, hydroxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, trifluoromethyl, trifluoromethoxy, C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{1-4}alkoxy, C_{1-4}alkanoyl, C_{1-4}alkanoyloxy, *N*-(C_{1-4}alkyl)amino, *N,N*-(C_{1-4}alkyl)$_2$amino, C_{1-4}alkanoylamino, *N*-(C_{1-4}alkyl)carbamoyl, *N,N*-(C_{1-4}alkyl)$_2$carbamoyl, C_{1-4}alkylS(O)$_a$ wherein a is 0 to 2, C_{1-4}alkoxycarbonyl, *N*-(C_{1-4}alkyl)sulphamoyl,

N,N-(C_{1-4}alkyl)$_2$sulphamoyl, and C_{1-4}alkylsulphonylamino; wherein R^6 and R^8 may be independently optionally substituted on carbon ~~by~~ with one or more R^{11} groups;

R^{10} is selected from halo, nitro, cyano, hydroxy, amino, carboxy, carbamoyl, mercapto, sulphamoyl, trifluoromethyl, trifluoromethoxy, C_{1-4}alkyl, C_{2-4}alkenyl, C_{2-4}alkynyl, C_{1-4}alkoxy, C_{1-4}alkanoyl, C_{1-4}alkanoyloxy, *N*-(C_{1-4}alkyl)amino, *N,N*-(C_{1-4}alkyl)$_2$amino, C_{1-4}alkanoylamino, *N*-(C_{1-4}alkyl)carbamoyl, *N,N*-(C_{1-4}alkyl)$_2$carbamoyl, C_{1-4}alkylS(O)$_a$ wherein a is 0 to 2, C_{1-4}alkoxycarbonyl, *N*-(C_{1-4}alkyl)sulphamoyl, *N,N*-(C_{1-4}alkyl)$_2$sulphamoyl, and C_{1-4}alkylsulphonylamino; wherein R^{10} may be independently optionally substituted on carbon ~~by~~ with one or more R^{16} groups;

R^7 and **R^9** are independently selected from C_{1-4}alkyl, C_{1-4}alkanoyl, C_{1-4}alkylsulphonyl, C_{1-4}alkoxycarbonyl, carbamoyl, *N*-(C_{1-4}alkyl)carbamoyl, *N,N*-(C_{1-4}alkyl)$_2$carbamoyl, benzyl, benzyloxycarbonyl, benzoyl, and phenylsulphonyl;

R^{11} and **R^{16}** are independently selected from halo, nitro, cyano, hydroxy, trifluoromethoxy, trifluoromethyl, amino, carboxy, carbamoyl, mercapto, sulphamoyl, methyl, ethyl, methoxy, ethoxy, acetyl, acetoxy, methylamino, ethylamino, dimethylamino, diethylamino, *N*-methyl-*N*-ethylamino, acetylamino, *N*-methylcarbamoyl, *N*-ethylcarbamoyl, *N,N*-dimethylcarbamoyl, *N,N*-diethylcarbamoyl, *N*-methyl-*N*-ethylcarbamoyl, methylthio, ethylthio, methylsulphinyl, ethylsulphinyl, mesyl, ethylsulphonyl, methoxycarbonyl, ethoxycarbonyl, *N*-methylsulphamoyl, *N*-ethylsulphamoyl, *N,N*-dimethylsulphamoyl, *N,N*-diethylsulphamoyl, and ~~or~~ *N*-methyl-*N*-ethylsulphamoyl;
or a pharmaceutically acceptable salt thereof;
with the proviso that said compound is not (*N*-methyl-*N*-butylsulphamoylmethyl)(phenyl)ketone; [1-(*N,N*-dimethylsulphamoyl)ethyl](phenyl)ketone; (*N,N*-dimethylsulphamoylmethyl)(4-nitrophenyl)ketone; (*N,N*-dimethylsulphamoylmethyl)(4-fluoro-2-methylaminophenyl)ketone; (*N,N*-dimethylsulphamoylmethyl)(3-methoxy-4-methyl-6-aminophenyl)ketone; (*N,N*-dimethylsulphamoylmethyl)(3-methoxy-6-aminophenyl)ketone; (*N,N*-dimethylsulphamoylmethyl)(phenyl)ketone; (*N,N*-dimethylsulphamoylmethyl)(2-nitro-4-methoxyphenyl)ketone; (*N,N*-dimethylsulphamoylmethyl)(2-amino-4-methoxyphenyl)ketone; [1-(*N*-methyl-*N*-butylsulphamoyl)ethyl](phenyl)ketone; or (*N,N*-dimethylsulphamoylmethyl)(thien-2-yl)ketone.

10. (Currently Amended) A pharmaceutical composition which comprises a compound ~~of~~

~~formula (I) or (Ia), or a pharmaceutically acceptable salt thereof, as claimed in either~~ of claims 8 or 9 in association with a pharmaceutically[[-]] acceptable diluent or carrier.

11-13. (Cancelled).

14. (Currently Amended) ~~The use~~A method for the treatment of a metabolic syndrome, comprising inhibiting 11βHSD1 according to claim 1 ~~of a compound as claimed in any one of claims 1-7 or 13 wherein production of, or producing an, 11βHSD1 inhibitory effect refers to the treatment of metabolic syndrome~~.

15. (Currently Amended) ~~The use~~A method for the treatment of diabetes, obesity, hyperlipidaemia, hyperglycaemia, hyperinsulinemia or hypertension, comprising inhibiting 11βHSD1 according to claim 1 ~~of a compound as claimed in any one of claims 1-7 or 13 wherein production of, or producing an, 11βHSD1 inhibitory effect refers to the treatment of diabetes, obesity, hyperlipidaemia, hyperglycaemia, hyperinsulinemia or hypertension, particularly diabetes and obesity~~.

16. (Currently Amended) ~~The use~~A method for the treatment of glaucoma, osteoporosis, tuberculosis, dementia, cognitive disorders or depression, comprising inhibiting 11βHSD1 according to claim 1 ~~of a compound as claimed in any one of claims 1-7 or 13 wherein production of, or producing an, 11βHSD1 inhibitory effect refers to the treatment of glaucoma, osteoporosis, tuberculosis, dementia, cognitive disorders or depression~~.

17. (Cancelled).